

Advances in regional anaesthesia: A review of current practice, newer techniques and outcomes

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ABSTRACT

Advances in ultrasound guided regional anaesthesia and introduction of newer long acting local anaesthetics have given clinicians an opportunity to apply novel approaches to block peripheral nerves with ease. Consequently, improvements in outcomes such as quality of analgesia, early rehabilitation and patient satisfaction have been observed. In this article we will review some of the newer regional anaesthetic techniques, long acting local anaesthetics and adjuvants, and discuss evidence for key outcomes such as cancer recurrence and safety with ultrasound guidance.

Key words: Adjuvants, erector spinae block, pectoral nerves block, quadratus lumborum block, regional anaesthesia, transversus abdominis block, ultrasound-guided

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INTRODUCTION

In the last decade, the practice of regional anaesthesia has advanced significantly, particularly following the introduction of ultrasound-guided regional anaesthesia (UGRA).^[1] In addition, benefits of regional anaesthesia on cancer recurrence and prevention of chronic post-surgical pain have gained focus in the recent years.^[2,3] In this article, we will review some of the newer regional anaesthetic techniques, long-acting local anaesthetics and adjuvants, and discuss evidence for key outcomes.

METHODS

In this narrative review, we examine the application of newer regional anaesthetic techniques and the evidence for ultrasound guidance. We (CW, AK, SP) performed a PubMed and Medline search for all published articles in English language since 2000, and predominantly included recent publications. We also manually checked missing articles from the above databases. We used keywords ‘ultrasound,’

‘ultrasound-guided,’ ‘quadratus lumborum (QL) block,’ ‘transversus abdominis block,’ ‘pectoral nerves (PECS block),’ ‘regional anaesthesia cancer recurrence,’ ‘erector spinae block’ and ‘diaphragm sparing blocks.’

REGIONAL ANAESTHESIA FOR CHEST WALL SURGERY

Studies have shown that paravertebral blocks (PVBs) can result in better post-operative analgesia with decreased opioid consumption, decreased length of stay and related side effects compared patient-controlled analgesia (PCA).^[4] A prospective observational study of patients undergoing major breast surgery under general anaesthesia showed that a

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single T4 PVB resulted in significantly decreased both dynamic and movement pain scores at rest up to 6 h post-operatively and decreased opioid consumption.^[5] However, not every patient may be a candidate for a PVB, particularly in the setting of anticoagulation or coagulopathy, and associated risks of pneumothorax, spinal cord trauma, neuraxial block and hypotension.

PECS blocks are novel plane blocks that involve infiltration of local anaesthetic between the muscles of the thoracic wall. The PECS I block is a superficial block performed between the pectoralis major and pectoralis minor muscles and targets the medial and lateral PECS.^[6] This block is ideally suited for superficial procedures such as the placement of breast expanders.

The modified PECS block or PECS II deposits local anaesthetic between the pectoralis minor and serratus anterior muscles at the level of the third rib and targets the lateral branches of the third to sixth intercostal nerves in addition to the long thoracic and thoracodorsal nerves.^[7] This provides more complete analgesia of the breast along the dermatomes of T2 to T4 and is ideal for wider breast excisions, mastectomies and procedures involving axillary dissections.

A randomised controlled trial comparing a combined PECS (I and II) blocks to control showed that the PECS block group had significantly lower pain scores, opioid consumption, and shorter post-anaesthesia care unit and hospital lengths of stay.^[8] Another randomised controlled trial comparing the combined PECS I and II block to a single injection PVB at T3 level showed that there was a significantly prolonged duration of analgesia in the PECS group as well as decreased opioid consumption.^[9] On the contrary, findings by Syal and Chandel demonstrate the superiority of ultrasound-guided PVB over PECS.^[10]

Blanco *et al.* described the serratus plane block, which deposits local anaesthetic above or below the serratus anterior muscle at the level of the fifth rib in the mid-axillary line.^[11] This results in dermatomal anaesthesia from T2 to T9 and maybe a more superficial block to perform compared to the PECS II. However, Gupta *et al.* have shown that serratus block is not superior to PVB in both quality of analgesia and opioid consumption for radical mastectomy.^[12]

Chronic pain after breast surgery is a common problem affecting 13%–49% of patients.^[13] Regional

techniques by reducing the intensity of acute pain have shown a trend towards decreasing the incidence of chronic intercostobrachial neuralgia and other subtypes of chronic pain, though further study is needed.^[5]

ADVANCES IN REGIONAL ANAESTHESIA FOR SHOULDER SURGERY

For decades, interscalene brachial plexus has been the gold standard; however, a significant number of patients develop hemidiaphragmatic paralysis (HDP) due to unilateral phrenic nerve blockade sometimes requiring respiratory monitoring. This is particularly important in patients with severe pulmonary disease and obese individuals. Lowering the local anaesthetic volume and deposition lateral to the brachial plexus is an attractive alternative, but this does not completely eliminate the risk. Other investigators have suggested a combination of supraclavicular brachial plexus approach with suprascapular nerve block. Tran *et al.*^[14] described infraclavicular block in combination with suprascapular nerve block (to cover the posterior aspect of shoulder joint) while Bansal *et al.* have suggested four individual nerve blocks to avoid HDP.^[15] With current discourse posing more questions, further studies are required to validate the efficacy of these blocks, and in this regard, studies are underway exploring various alternatives.

Recently, costoclavicular approach to brachial plexus has been described. Cadaver studies reveal that the three cords lie in close proximity lateral to axillary artery and vein in a triangular fashion in the costoclavicular space, which is located deep and posterior to the midpoint of the clavicle. Although the benefits of this approach are similar to supraclavicular block, the risk of pneumothorax and sparing of lower trunk nerves is lower. This block is particularly useful for vascular, wrist and hand surgeries.

REGIONAL ANAESTHESIA FOR ABDOMINAL WALL SURGERY

For those patients who may not be ideal candidates for neuraxial anaesthesia, truncal blocks are an attractive multimodal approach to pain control for a variety of abdominal surgeries.

Transversus abdominis plane block

Transversus abdominis plane (TAP) infiltration has become an increasingly popular option for both

ambulatory and inpatient abdominal procedures and provides analgesia to the parietal peritoneum and anterior abdominal wall.^[16,17] TAP blocks were previously performed through a landmark technique, but the introduction of an ultrasound-guided approach has allowed for real-time visualisation of the needle as well as local anaesthetic spread.^[18]

The traditional or posterior approach uses a transversely oriented ultrasound on the anterolateral abdominal wall to identify the TAP between the internal oblique and transversus abdominis muscles. Local anaesthetic spread in the TAP can be observed and typically covers the anterior rami of T9 to L1. This block is appropriate for incisions that are largely below the level of the umbilicus. The oblique subcostal approach can be used for the upper abdominal surgeries. With this approach, the needle is inserted near the xiphoid and advanced inferolaterally to deliver local anaesthetic in the TAP along the costal margin. This method can be combined with the posterior approach to provide even wider analgesic coverage.

There are several limitations and areas of on-going understanding. A study in healthy volunteers showed that the cutaneous sensory extent of spread with TAP blocks is variable and non-dermatomal, likely due to variation in anatomy.^[19] There is no consensus on ideal volume or concentration of local anaesthetic, with clinical studies using volumes from 10 to 30 mL per side.^[16] As compared to a peripheral nerve block that targets a specific nerve, this is a field block in an anatomic plane where spread of local anaesthetic is the primary driver of analgesic effect.^[20] Therefore, it is critical in TAP block that the deposition of local anaesthetic occurs in the correct plane and the spread is visualised in real time.

There have been many studies assessing the efficacy of TAP blocks with variable outcomes.^[21] Subcostal TAP catheters utilising an intermittent bolus protocol showed similar pain control as epidurals in patients undergoing upper abdominal surgery.^[22] Most studies show that TAP blocks have a positive effect on analgesia, with one study also showing a beneficial effect on post-operative respiratory mechanics.^[23] A recent meta-analysis showed that TAP blocks decrease opioid consumption at 6 and 24 h post-operatively.^[24] However, in this analysis, there was no difference in analgesic effect in patients who received intrathecal long-acting opiates.

Rectus sheath block

Rectus sheath blocks provide analgesia for umbilical and other midline surgical incisions by blocking the terminal branches of the T9 to T11 intercostal nerves. There have been multiple reports of successful use of rectus sheath blocks for a variety of abdominal surgeries, including umbilical and inguinal hernia repair, laparoscopic cholecystectomy, laparoscopic appendectomy and pyloromyotomy, with some case reports citing the use of the rectus sheath block as the primary anaesthetic technique.^[25] A meta-analysis showed that rectus sheath blocks have small but significant reductions in pain scores, opioid requirements and time to rescue analgesia in paediatric patients.^[26]

Quadratus lumborum block

Local anaesthetic deposited in the plane between the QL muscle and the medial layer of the thoracolumbar fascia can provide relief of somatic pain in the upper and lower abdomen. Due to the more dorsal injection point and potential spread to the paravertebral space, QL blocks can cover more extensive dermatomes for a significantly longer duration of analgesia as compared to TAP blocks.^[27] However, there is variation in nomenclature and precise location of the needle tip, with anterior, lateral and posterior approaches among others described in the literature^[28] [Figures 1 and 2]. Depending on the approach and the location of deposition of local anaesthetic, QL block has been clinically described as QL1 (injection lateral to the QL muscle), QL2 (injection posterior to QL muscle)

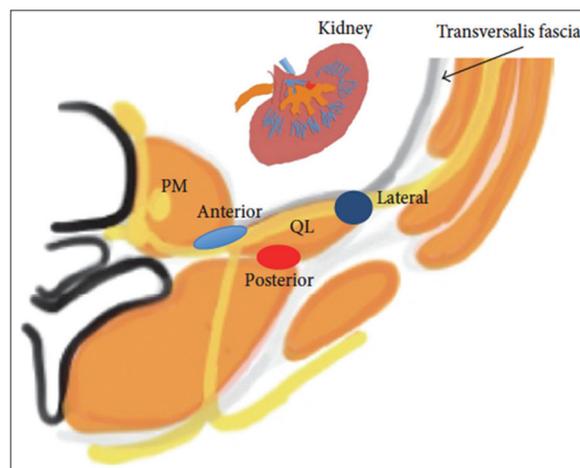


Figure 1: Anatomic view of quadratus lumborum. The lateral (quadratus lumborum 1), posterior (quadratus lumborum 2) and anterior (quadratus lumborum 3) approaches. PM: Psoas major muscle and grey line is transversalis fascia. Adapted with permission from Ueshima *et al.* -BioMed Research International (open access) Vol 2017, doi 10.1155

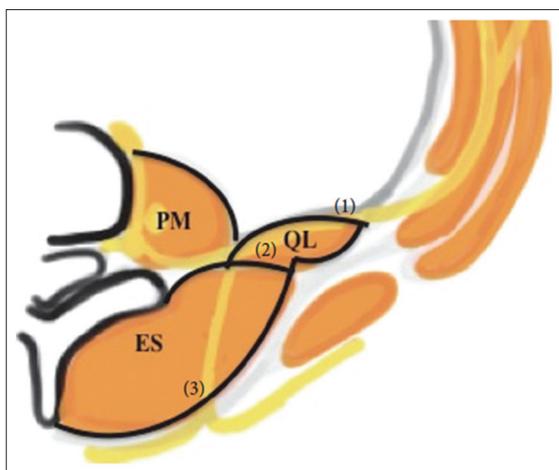


Figure 2: Anatomic view of thoracolumbar fascia. The thoracolumbar fascia is divided into three layers, anterior (1), middle (2) and posterior (3). QL: Quadratus lumborum, ES: Erector spinae, LD: Latissimus dorsi. Adapted with permission from Ueshima *et al.* - BioMed Research International (open access) Vol 2017, doi 10.1155

and QL3 block (injection between anterior surface of QL muscle and psoas major). However, evidence is sparse as to the clear clinical benefit of different approaches, until newer studies reveal improved quality of analgesia. There is some evidence to show that QL blocks provide visceral analgesia due to more medial spread into lumbar paravertebral space. It is important to note that all patients receiving QL blocks are at risk of developing quadriceps weakness (and falls) secondary to blockade of lumbar plexus.

Erector spinae plane block

Erector spinae plane (ESP) block is an interfascial plane block that entails deposition of local anaesthetic deep to erector spinae muscle adjacent to transverse processes. A single injection of 20 ml of 0.5% ropivacaine at T5 level (3 cm from the midline) can result in sensory blockade from T3 to T9 over posterior thorax and T3 to T6 anterolateral thoracic area by blocking the ventral and dorsal rami of the thoracic spinal nerves.^[29] In cadaver studies, it has been shown that the dye spreads both caudally and cephalad to cover multiple levels.^[29] The most common indication is acute post-thoracotomy pain and chest wall trauma, but bilateral lower thoracic injection at T8 levels have been successfully used for the effective analgesia for open abdominal and bariatric surgeries.^[30,31] The efficacy of ESP block for incisional pain remains to be confirmed in larger clinical studies. Currently, very few case reports have been reported in the literature.

Regional anaesthesia for knee surgery: Adductor canal block

Moderate-to-severe pain associated with total knee replacements can remain for at least the first 48–72 h in the post-operative period. Femoral nerve block (FNB) has become a common and highly effective method to control post-operative pain in this population. It also avoids risks associated with epidural anaesthesia and does not prohibit deep vein thrombosis prophylaxis. In recent years, the adductor canal block (ACB) has become an attractive alternative to FNB due to its quadriceps-sparing activity to facilitate early rehabilitation programme.

A double-blind randomised, controlled study comparing FNB versus ACB showed that ACB caused less motor weakness at 6 and 8 h post-operatively. They found ACB to be non-inferior in providing analgesia.^[32] As the primary benefit of the ACB is less quadriceps weakness, it is necessary to determine if this benefit decreases at higher volumes of local anaesthetic. Bilateral ACB on healthy volunteers, using 10 mL of 0.1% ropivacaine on one side and 30 mL on the contralateral side showed no difference in sensory block or quadriceps strength. Of note, 4 participants out of 26 experienced a reduction in quadriceps strength by greater than 25% at both volumes.^[33] A recent meta-analysis also showed either improved quadriceps function with ACB or no difference compared to FNB up to 48 h. However, there seems to be lack of consensus on site of injection for the ACB.^[34]

Burckett-St Laurant *et al.* set out to define the optimal site of ACB. They performed cadaveric dissections of 20 lower limbs and examined branches of both the femoral and obturator nerves along the adductor canal. They found the nerve to the vastus medialis (NVM) plays a more important role than previously thought to the innervation of the anteriolateral compartment of the knee. For this reason, ideal injection site seems to be the midportion of the adductor canal (the midpoint between the proximal and distal ends) as it is high enough to block the saphenous nerve and transmuscular branches of the NVM, but distal enough to avoid spread to the femoral triangle.^[35] While further studies are needed with a more standardised definition of site of the ACB, the current research suggests that ACB offers an improvement in quadriceps function compared to FNB with non-inferior pain control.

In most patients, because the posterior capsule is not intersected during surgery, pain from the posterior

aspect is described to be referred from intra-articular nerves, but the posterior branch of the obturator nerve also supplies the knee capsule posteriorly, and therefore, for complete analgesia obturator nerve block should be considered.^[36] That being said, surgeons often perform periarticular local infiltration intraoperatively with good results, avoiding the need for sciatic nerve block.^[37] Alternatively, pre-operative ultrasound-guided injection of the capsule with 15-20 mL of long-acting local anaesthetic can be accomplished.

LONG-ACTING LOCAL ANAESTHETICS

The advent of long-acting local anaesthetics may provide an opportunity to decrease or even eliminate the use of nerve catheters, and in this regard, liposomal bupivacaine has been shown to increase the duration of action as well as decreased peak plasma concentrations compared to plain bupivacaine. It has been shown to significantly reduce pain in the first 72 h post-operatively, decrease opioid requirements and improve patient satisfaction compared to placebo in haemorrhoidectomy, bunionectomy, local infiltration analgesia of the knee and other surgical site infiltration.^[38] However, use of liposomal bupivacaine has resulted in unreliable dose-response relationships in FNBs and limited prolongation of sensory effect in epidurals. Liposomal bupivacaine is currently approved for local infiltration only.

ADJUVANTS TO REGIONAL ANAESTHESIA

As is it not always feasible to send patients home with indwelling peripheral nerve catheters, there is still a need for methods to increase the duration of analgesia with single-shot peripheral nerve blocks.

Perineural dexamethasone

Dexamethasone is believed to work by reducing release of inflammatory mediators and by inhibiting potassium channel-mediated discharge of C-fibres. One of the first placebo-controlled human studies examined patients undergoing forearm surgery under 90 min in length who received an axillary block for the procedure. The control arm of the study received a block with 1.5% lidocaine while the study arm received 1.5% lidocaine (with 4mg/mL dexamethasone). The results showed the dexamethasone-treated group had both a longer duration of sensory and motor blockade compared to control.^[39]

With initial promising results, nine placebo-controlled, randomised studies were examined in a recent systematic review and meta-analysis evaluating the effect brachial plexus blockade with dexamethasone and confirmed that dexamethasone (at doses of 8-10mg) increased the duration of the sensory block when using intermediate-acting and long-acting local anaesthetics by 3 h and 10 h, respectively. Despite sensory block prolongation, no statistical difference was noted in opioid consumption.^[40]

Recent studies have examined whether intravenous dexamethasone provides similar block prolongation compared to perineural administration.^[41] Rahangdale *et al.* compared dexamethasone 8 mg given intravenously or through perineural injection in sciatic nerve blockade to placebo. The results showed no statistically significant difference in the quality of recovery score at 24 h or 2 weeks post-operatively. In addition, despite lower pain scores in the first 24 h among the perineural dexamethasone group, there was no difference in post-operative opioid use among the three groups. Both dexamethasone groups showed statistically significant longer time to first toe movement compared to placebo, while only the perineural group showed a significantly longer analgesia duration.^[42]

Perineural dexmedetomidine

Dexmedetomidine, an α_2 agonist, which has eight times more affinity for α_2 than α_1 (compared to clonidine)^[43] can prolong sensory block. When compared with a placebo in posterior tibial block dexmedetomidine (1 μ g/kg) showed a statistically significant increase in duration of sensory blockade in the dexmedetomidine group by a mean 5.3 h. However, the study group showed a statistically significant lower blood pressure starting at hour 1 and lasting until hour 8 after the block.^[44]

While longer sensory block times can be helpful, more important is a longer duration of analgesia and improved pain scores. Bharti *et al.* evaluated the use of perineural dexmedetomidine in supraclavicular blocks for patients undergoing upper limb and hand surgeries. Their two arms consisted of equal part 2% lidocaine and 0.75% ropivacaine with 1:200,000 epinephrine with and without 1 mcg/kg dexmedetomidine. They found the nerve block with dexmedetomidine significantly increased median duration of motor block, sensory block and analgesia by 3, 4 and 5 h, respectively.^[45] However, increased adverse effects such as bradycardia and sedation have been reported in other studies.^[46,47]

Despite a number of studies that have shown no negative effects of perineural injection of dexmedetomidine, the IV route of administration is the only route approved by the FDA. To determine if there was an advantage to using perineural versus intravenous dexmedetomidine, Abdallah *et al.* compared interscalene block for shoulder arthroscopy with placebo to either 0.5 mcg/kg perineural or intravenous dexmedetomidine. Both dexmedetomidine groups had statistically significant longer times to the first report of pain and decreased 24-h opioid requirements. No statistical difference was noted between the two groups.^[48]

While the above results suggest a central-acting mechanism of action for the prolongation of peripheral nerve blockade with dexmedetomidine, other studies suggest a peripheral mechanism of action. Andersen *et al.* studied 21 healthy volunteers by performing bilateral saphenous nerve blocks, using 0.5% ropivacaine with 100-mcg dexmedetomidine one on side and plain 0.5% ropivacaine on the other. They found a clinically significant increase in the mean duration of sensory blockade in the ropivacaine plus dexmedetomidine group compared to the control group. Their findings suggest a possible peripheral site of action for perineural dexmedetomidine.^[49] That being said, further studies are needed to evaluate the mechanism of action of perineural dexmedetomidine.

EVIDENCE FOR ULTRASOUND-GUIDED REGIONAL ANAESTHESIA

Although it has not been shown that ultrasound meaningfully affects the incidence of peripheral nerve injury, the growing use of ultrasound technology in regional anaesthesia does have several possible advantages in comparison to nerve stimulator or landmark techniques. The use of ultrasound leads to faster sensory block onset, fewer vascular punctures, faster performance time and fewer needle passes in upper extremity blocks.^[1] In supraclavicular blocks, ultrasound guidance has decreased the frequency of pneumothorax though caution is still mandated during this procedure. UGRA also reduces but does not eliminate the incidence and severity of hemidiaphragmatic paresis through the use of decreased local anaesthetic volumes. In lower extremity blocks, ultrasound improves onset of sensory block and performance time. Importantly, registry data indicates that UGRA significantly reduces the incidence of local anaesthetic systemic toxicity by up to 65% compared to other nerve localisation methods.^[1] These safety

implications may further encourage more anaesthesia practitioners to employ ultrasound technology in their practice.

REGIONAL ANAESTHESIA AND CANCER RECURRENCE

Cancer recurrence and survival after primary surgery is impacted by a number of different factors, including the response of the immune system. Pre-operative anxiety, intraoperative hypothermia, blood transfusion, general anaesthesia and pain have all been shown to negatively affect immunologic response.^[50] In addition, both exogenous and endogenous opioids have been shown to promote tumour growth by inducing mitogenesis and angiogenesis.

One of the first studies to compare opioid versus regional anaesthetic analgesia was performed by Exadaktylos *et al.* They performed a retrospective analysis of women undergoing primary mastectomy and axillary dissection for breast cancer. The two groups consisted of those who had a paravertebral catheter for post-operative analgesia versus those who had morphine PCA. The metastases-free survival was 94% and 82% at 24 months and 94% and 77% at 36 months for the paravertebral group and morphine PCA group, respectively.^[2]

Despite initial promising results, there have been a number of studies that show conflicting results. A more recent retrospective analysis compared women undergoing surgery for breast cancer stages 0-III over a 9-year period. Women received either general anaesthesia or sedation with paravertebral regional anaesthesia. No difference was noted between overall survival, disease-free survival or local-regional recurrence.^[51] On the contrary, in a cohort study of >42,000 patients undergoing surgery for colorectal cancer, Cummings *et al.* found epidural anaesthesia was associated with an increased 5-year survival (61% compared to 55%) compared to those who did not have an epidural. However, no difference was seen in cancer recurrence rates between the two groups.^[52]

Various studies have been published evaluating the effect of regional anaesthesia on a number of different cancer types. In a recent systematic review and meta-analysis, a total of 20 studies were evaluated, and they found perioperative regional anaesthesia use was associated with improved overall survival but not with reduced cancer recurrence.^[3]

Despite some evidence suggesting a survival benefit of regional anaesthesia, at this point, there is not enough evidence to truly answer the question. A large number of randomised, controlled studies are needed to determine if regional anaesthesia does provide a survival advantage during cancer surgery and if it is specific to different types of cancer.

ENHANCING SAFETY IN REGIONAL ANAESTHESIA

Intraneural injection

The controversial method of intraneural/intrafascicular injection to enhance onset and duration of block is generally not advisable because of potential neurotoxicity and consequent histological changes in peripheral nerves. Whether these changes result in clinical neurological deficit is not clearly understood. Hara *et al.* noticed a 16% incidence of unintentional subgluteal sciatic nerve (intraneural) injection that hastened the onset of the block, but did not affect the duration of the block. Interestingly, no patients developed post-operative neurological complications.^[53] Similarly, in a randomised controlled trial of intraneural injection a reduction in the amplitude of action potential was noticed at 5 weeks, but at follow-up at 6 months none of the patients reported any neurological symptoms.^[54] Histological nerve injury has been demonstrated when minimum stimulating current is <0.2 mA, but this does not reliably predict the distance of the needle tip from the nerve, and therefore may not confirm intraneural placement. On the contrary, ultrasound guidance reveals nerve expansion predicting histologic injury when intraneural injection is placed; again this does not always translate to functional injury.^[55]

Injection pressure monitoring

While investigators seek ways to mitigate the risk of nerve injury due to unintentional intrafascicular injection various safety techniques such as real-time visualisation by ultrasound guidance, stimulation technique and injection pressure monitoring device^[56] are used. The ideal method to enhance safety appears to be a combination of all the three methods. Although injection pressure monitoring devices are easily available and inexpensive, their widespread use is not observed in routine clinical practice.^[57]

SUMMARY

The practice of regional anaesthesia has advanced rapidly in recent years with the application of

ultrasonography resulting in significant improvement in quality of nerve blocks and patient satisfaction. Although adjuvants such as dexamethasone have shown prolongation of duration of block their widespread use in routine practice has not been observed. While regional anaesthesia is effective for the adequate management of acute pain, its beneficial effect on the development of chronic pain and cancer recurrence needs further research.

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There are no conflicts of interest.

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